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Table of Contents

Cover.....	1
SF 298.....	2
Table of Contents.....	3
Introduction.....	4
Personnel.....	4
Equipment.....	4
Programs.....	5
Publications.....	7
Committees and Honors.....	11
GPCC Scientific Retreat.....	12

The Dean and Betty Gallo Prostate Cancer Center

Annual Report

July 1, 2001 – June 30, 2002

The Dean and Betty Gallo Prostate Cancer Center (GPCC) has developed in the past 12 months in the areas of basic science, translational research, education, outreach and behavioral studies. Over the past 12 months the GPCC has published one book, 17 peer-reviewed manuscripts with 11 submitted, 15 abstracts, and obtained 5 new federally funded grants with 3 grants pending. As planned, we successfully initiated programs including our center retreat, a prostate cancer workshop as part of the Cancer Institute of New Jersey (CINJ) state-wide retreat, pilot grant program, research working groups and new community partnerships for education and outreach.

PERSONNEL

The center has recruited a translational laboratory technician, three postdoctoral fellows, a program assistant, and is actively recruiting a pathologist.

Because of the growth of GPCC, the Cancer Institute of New Jersey is adding value by recruiting additional clinical research personnel. CINJ is recruiting a GU medical oncologist to assist with patient care and clinical research programs. CINJ will also support a full-time urologist dedicated to the programs of GPCC. CINJ has supported additional personnel to expand the clinical research program under Dr. Robert DiPaola including two data managers and one clinical research nurse. One of the present advanced practical nurses has become full-time and has assumed administrative responsibilities at GPCC.

The basic research program staff has expanded through outside support by hiring a postdoctoral fellow (Dr. Ouyang), a new graduate student (Anna Puzio) and a medical student (Daniel Lee) to perform developmental basic science research as part of GPCC. Another example is the assistance provided by the DOD for the salary support a research specialist (Sandy Price) for the development of transgenic models for prostate cancer that will provide the basis for a program project submission focused on prostate carcinogenesis. One such model is being developed as a collaborative effort by Drs. Michael Shen and Danny Reinberg will model metastases in mutant mice.

EQUIPMENT:

The new equipment for the Transgenic Facility has been installed. The Clinical Research laboratory under the direction of Dr. Robert DiPaola has expanded their capabilities with the addition of the new centrifuge and refrigerator.

GPCC BASIC SCIENCE PROGRAM

Funding from the DOD for the basic science program of the Gallo Prostate Cancer Center has enabled us to expand our programs in translational research and has also enhanced our competitiveness for peer-reviewed grant funding. One new federally funded grant in basic science was obtained in this grant period. In particular, Dr. Gao, a post-doctoral fellow funded by the DOD, has been developing a pre-clinical trials program that will foster interactions between the basic and clinical research programs. In collaboration with Dr. DiPaola and the clinical research program, Dr. Gao has been utilizing the mouse models of prostate cancer, developed by Dr. Abate-Shen and members of the basic science program, to develop new treatment regimes for prostate cancer patients. The basic program published 5 manuscripts during this grant period.

Dr. Hait was awarded a DOD grant entitled "Regulation of Drug Sensitivity by Functional Status of p53 in Human Prostate Cancer". The major goals of this project are to assess the role of p53 in creating the multidrug resistance phenotype in human prostate cancer and determine whether restoration of p53 function can restore drug sensitivity.

GPCC CLINICAL RESEARCH PROGRAM

Due to the support of the DOD, the clinical research program has shown tremendous growth over the past year. We have 14 active clinical trials and accrued 70 patients on GU clinical trials in 2002. Two federally funded clinical grants were awarded. The clinical program published 12 manuscripts during this grant period. A trial for hormone refractory prostate cancer opened with funding by the DOD peer-reviewed grant process under Dr. DiPaola. A second trial was recently funded by the NIH-CAM as a pilot project for patients with rising PSA after local therapy. Dr. Kumar (Radiation Oncology) was funded by the GPCC to conduct a trial combining chemotherapy with radiation therapy. With additional funding the staff now includes an Assistant Clinical Director, 2 clinical research nurses, two data managers and two postdoctoral fellows. The group continues to meet weekly to discuss current trials, patient enrollment and future trial ideas. This program has expanded into the GU Clinical Trials Alliance which includes all of the partners and affiliates of CINJ in order to open enrollment to as many eligible patients as possible in New Jersey.

EDUCATION PROGRAMS

RETREAT:

GPCC sponsored a retreat on December 8th in which 13 investigators participated by presenting their research in prostate cancer. The topics ranged from a discussion of clinical trials to basic studies on prostate development. The retreat was very well attended by members of the community (see program at end of report).

GPCC SYMPOSIUM AT CINJ STATE-WIDE RETREAT

GPCC sponsored a Prostate Cancer Workshop on April 24, 2002 as part of the CINJ state-wide cancer retreat in Princeton, New Jersey. The lecturers were Dr. Philip Kantoff, Director, The Lank Center for Genitourinary Oncology and Associate Professor of medicine at Dana-Farber Cancer Institute; Dr. Angelo DeMarzo, Assistant Professor of Pathology at John Hopkins Medical Institutions and Dr. Gerald Cunha, Professor of anatomy and urology at University of California at San Francisco.

RESEARCH WORKING GROUPS

GPCC sponsors Research Working Groups to bring together researchers interested in prostate cancer to present their work and encourage collaborations. Presentations were given by Drs. Robert DiPaola, Deidre Nelson, Ramsey Foty, Longqin Hu and Robert Weiss.

PILOT GRANT PROJECT PROGRAM

GPCC sponsored a pilot grant program which is aimed at encouraging new research in prostate cancer. We received a total of 16 grant applications, 3 of which were from postdoctoral candidates. A panel of noted scientists was assembled to review the grants. We awarded four pilot project grants. One additional researcher who submitted their project to GPCC was awarded funded from CINJ under the Centers of Excellence program. The funded projects are:

Effect of 12-0-tetradecanoylphorbol-13-acetate (TPA) on the growth of prostate tumors submitted by Dr. Alan Conney

Genetic studies of IGE BP function during prostate tumorigenesis submitted by Dr. John Pintar

Phase I/II Trial of neoadjuvant 13-cis-retinoic acid and alpha-interferon prior to definitive three-dimensional conformal radiation therapy for high risk localized adenocarcinoma of the prostate submitted by Dr. Parvesh Kumar.

Regulation of the putative tumor suppressor ICER in prostate cancer by PTEN and P13K signaling submitted by Dr. Carlos Molina (Funded under CINJ Centers of Excellence Program)

Novel Aminotriazole Derivatives as Inhibitors of Prostate Tumor Cell Growth submitted by Dr. Anna M. Vetrano (declined after receiving NIH Postdoctoral Fellowship)

CANCER CONTROL AND OUTREACH PROGRAM

The Outreach and Education Programs with the 100 Black Men of New Jersey have been very successful and have allowed us to expand a behavioral health program into additional underserved communities in New Jersey. In 2002 we initiated a clinical trial to test the hypothesis that culture subgroups within African American men influence their understanding of clinical trials and prostate cancer. Our specific research goals are to test the following hypothesis:

- 1) Black men from different ethnic groups (i.e. African-American men from the southern United States, African-American men from the northern United States, men of African descent, and men of Caribbean descent) differ in their beliefs about prostate cancer, prostate cancer screening and treatment, and in other factors and beliefs that impact screening behavior (e.g. cynicism, social networks, and beliefs about medical research).
- 2) Black men from different ethnic groups differ in their willingness to undergo screening for prostate cancer.

3) The different rates of screening predicted for black males with different ethnic backgrounds can be attributed to differences in beliefs (e.g. believing screening is effective) and social networks (e.g. knowing someone with prostate cancer).

In 2002 we have over 50 educational programs and 6 village gatherings planned.

Through a new partnership with the Jewish Renaissance Foundation Medical Center in Perth Amboy, the first faith-based minority medical center under President Bush's new health initiative the center has expanded their program into the Latino and Asian community.

In partnership with the Latino Physicians Group at one of CINJ's partners and affiliates we have participated in additional education programs in the Latino Community.

During fiscal year 2002 we participated in over 50 prostate cancer educational programs. In cooperation with the 100 Black Men of New Jersey besides our regular programs 6 village gatherings were held in the underserved community.

RECENT PUBLICATIONS

Cunha, G.R., Donjacour, A.A., Hayward, S.W., Thomsen, A., Marker, P., Abate-Shen, C., Shen, M.M., and Dahiya, R. (2002). Cellular and molecular biology of prostatic development. In Prostate Cancer (Kantoff, P.W., Carroll, P., D'Amico, Eds), A. Lippincott, Williams and Wilkins, Philadelphia, PA, pp. 16-28.

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- DiPaola, R.S., Patel, J., and Rafi, M.M. (2001). Targeting Apoptosis in Prostate Cancer. *Hematology/Oncology Clinical of North America* 15:3:509-524.
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- Eid, J.E., Brunner, M., Segal, L., Cummings, K.F., Weiss, R.E., Goodin, S., Todd, M., Aisner, J., and DiPaola, R.S. (2001) Effect of P-30 Protein and Tamoxifen on TGF-Betal and IGF-1 in Patients with Prostate Cancer, *Urologic Oncology* 6:243-247.
- DiPaola, R.S., Rinehart, J., Nemunaiti, J., Effinghaus, S., Rubin, E., Capanna, T., Ciardella, M., Fontaine, M., Adams, N., Williams, A., Schwartz, M., Winchell, G., Wickersham, K., Duetsch, P., and Yao, S. (2002) Characterization of a novel prostate specific antigen activated peptide-doxorubicin conjugate in patients with prostate cancer. *Journal of Clinical Oncology* April 1:20(7):1874-1879.
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- DiPaola, R.S. (2002) To Arrest or not G2-M cell cycle arrest. The Biology Behind. *Clin Cancer Res*, 3311-4, 2002.
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Grzywacz, M.J., Yang, J.M. and Hait, W.N. Effect of overexpression of the multidrug resistance protein (MRP1) on the transport of the antiandrogen flutamide. *Cancer Research*. (Manuscript submitted).

Grzywacz, M.J., Yang, J.M., and Hait, W.N. The active metabolite of flutamide, 2-hydroxyglutamide, is a substrate for MRP1. *Proc. Amer. Assoc. Cancer Res.* (Manuscript submitted).

BOOKS

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RECENT ABSTRACTS

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Rafi, M.M., Vastrano, B.C., Rosen, R.T., Ghai, G., Ho, C.T., and DiPaola, R.S. (2002) Novel compound isolated from Vietnamese coriander by bioassay directed fractionation induces bcl-2 phosphorylation and apoptosis. *American Association for Cancer Research* 43:1037.

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Goodin, S., Rao, K., Engle, E., Kane, M., Capanna, T., Ciardella, M., Todd, M., and DiPaola, R.S. (2002) A phase II study of docetaxel and vinorelbine in hormone refractory prostate cancer (HRPC) with and without prior chemotherapy. PASCO Abstract #2459.

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Abate-Shen, C., Kim, M.J., Desai, N., Bhatia-Gaur, R., Banach-Petrosky, W., Parson, R., Cardiff, R.D., and Shen, M.M. (2001) Cooperativity of tissue-specific and broad-spectrum tumor suppressor genes in a mouse model of prostate cancer. Modeling Human Prostate Cancer in Mice (The Jackson Laboratories, ME).

NEW COMMITTEES

Dr. Robert S. DiPaola

March 2002 elected as Chairman of the New Jersey Oncology Group (NJOG), our Statewide clinical trials network, at The Cancer Institute of New Jersey

June 2002 named Co-Chair of the Genitourinary Group at the Eastern Cooperative Oncology Group (ECOG)

June 2002 named member of the Grant Study Section of the Department of Defense (DOD) for both Clinical and Experimental Therapeutics-2 in Prostate Cancer

Dr. Cory Abate-Shen

July 2001 UCSF Mini-Symposium on Mouse Models of Angiogenesis, San Francisco, CA

October 2001 Meeting Organizer, Mouse Models of Prostate Cancer, Bar Harbor, MI

March 2002 Huntsman Cancer Institute at the University of Utah, Salt Lake City, Utah

Betty Gallo

Member of State of New Jersey Commission on Cancer Research IMPACT Committee (Promotion of clinical trials in underserved population)

HONORS

Betty Gallo

February 2002 received CBS "Fulfilling the Dream" award in honor of Dr. Martin Luther King for her work in the underserved population.

*GPCC Scientific Retreat
December 8, 2001*

8:30	Cory Abate-Shen	Introduction
8:35	Robert DiPaola	Translational Research in Prostate Cancer
8:50	Parvesh Kumar	A Novel Therapeutic Strategy Testing the Safety and Feasibility of Concurrent Docetaxel and 3-D Conformal Radiation Therapy in patients with High-Risk Localized Adenocarcinoma of the Prostate: Progress Report of an On-going Phase I/II Trial
9:05	Tamara Minko	Enhancing the Efficacy of Chemotherapeutic Drugs by the Suppression of Antiapoptotic Cellular Defense
9:20	Steve Marcella	PSA Screening and Prostate Cancer Mortality: Preliminary Evidence of Increased Incidence of Prostatism in Clinically Aggressive Prostate Cancer
9:35	Carlos Molina	Regulation of the Transcriptional Repressor Inducible cAMP Early Repressor in Prostate Cancer Cells
9:50	Keith Bupp	Targeting Retrovirus Using random Display envelope Libraries
10:05	Stuart Lutzker	Abrogation of the Mitotic Spindle-checkpoint in Prostate Cancer Cells and Sensitivity to Antimicrotubule Drugs
10:20	John Pintar	Searching for Prostate Abnormalities in IGFBP KO Mice
10:35	Arnold Rabson	Mechanisms of Constitutive NF- κ B Activation in Human Prostate Cancer Cells
10:50	Bill Hait	Molecular Determinants of Response to Therapy in Patients with Prostate Cancer
11:05	Zui Pan	Ca ²⁺ Signaling and Bax Translocation in Apoptosis of Prostate Cancer Cell Lines
11:20	Mike Shen	Molecular Determinants of Response to Therapy in Patients with Prostate Cancer
11:35	Cory Abate-Shen	Cooperativity of Tissue-Specific and Broad-Spectrum Tumor Suppressor Genes in a Mouse Model of Prostate Cancer